P T 61812

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: Natalie Davis Serial Number: 09/619285

Date: 3/6/02 Phone: 308-6410 Art Unit: 1642

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Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search claims 28-34 as they relate to a nucleic acid encoding a chimeric serum albumin protein + a delivery vector comprising one of the vectors of claim 31. Also, for transfected cells of claim 33 that have been exposed to the delivery vector of claim 31.

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

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— chimeric polypeptides of serum albumin

Gyuris, J Lamphere, L Morris, A

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Search Site		Vendors	
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	A.A. Sequence		SDC
	Structure		DARC/Questel
8	Bibliographic		Other

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Gyuris et al.

Serial No: 09/619,285

Filed: July 19, 2000

For: Chimeric Polypeptides of Serum Albumin and Uses Related Thereto

Attorney Docket No. GPCI-P01-109

Art Unit: 1642

Examiner: Natalie A. Davis

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail, postage prepaid, in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231 on the date indicated below:

December 20, 2001
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Dawn Harmon
Dawn Harmon

Assistant Commissioner of Patents
Washington, D.C. 20231

REPLY TO RESTRICTION REQUIREMENT

Sir:

Please kindly enter the following amendments.

In the claims:

For the convenience of the Examiner, all elected claims (28-34 and 49-83), whether or not amended, are presented below.

28. (**Amended**) A nucleic acid encoding a chimeric polypeptide comprising serum albumin protein (SA) having a biologically active heterologous peptide sequence inserted into at least one region selected from residues 360-369 and residues 450-463, optionally replacing one or more residues of the region into which it is inserted.

A 1

29. (**Amended**) A delivery vector comprising the nucleic acid of claim 28, 49, or 50.

30. (**Reiterated**) The delivery vector of claim 29, wherein said delivery vector comprises a virus or retrovirus.

31. (**Amended**) The delivery vector of claim 30, wherein said virus or retrovirus is selected from adenoviruses, adeno-associated viruses, herpes simplex viruses, human immunodeficiency viruses, or vaccinia viruses.

A2

32. (**Reiterated**) Transfected cells comprising target cells which have been exposed to the delivery vector of claim 29.

33. (**Amended**) The transfected cells of claim 32, wherein the cells are selected from blood cells, skeletal muscle cells, stem cells, skin cells, liver cells, secretory gland cells, hematopoietic cells, or marrow cells.

A3

34. (**Amended**) A pharmaceutical preparation comprising a pharmaceutically acceptable excipient and the chimeric polypeptide encoded by the nucleic acid of claim 28, 49, or 50.

48. (**Amended**) A method for modulating one or more of cell proliferation, cell differentiation, and cell death in an organism, comprising:

A4

(i) providing a delivery vector comprising genetic material which encodes the chimeric polypeptide of claim 1, 2, or 3; and

(ii) introducing said vector into target cells in vivo, under conditions sufficient to induce said target cells to express said polypeptide.

Please add the following new claims:

49. (**New**) A nucleic acid encoding a chimeric polypeptide having the structure A-B-C, wherein:

A5

A represents an N-terminal peptide fragment of serum albumin (SA) terminating in an amino acid corresponding to one of residues 359-368;

B represents a biologically active heterologous peptide sequence; and,

C represents a C-terminal peptide fragment of SA beginning from an amino acid corresponding to one of residues 361-370;

wherein A and C do not include overlapping portions of the regions 360-369 and 450-463.

50. (New) A nucleic acid encoding a chimeric polypeptide having the structure A-B-C, wherein:

A represents an N-terminal peptide fragment of serum albumin (SA) terminating in an amino acid corresponding to one of residues 449-462;

B represents a biologically active heterologous peptide sequence; and,

C represents a C-terminal peptide fragment of SA beginning from an amino acid corresponding to one of residues 451-464;

wherein A and C do not include overlapping portions of the regions 360-369 and 450-463.

51. (New) The nucleic acid of claim 28, 49 or 50, wherein the heterologous peptide sequence comprises a fragment of an angiogenesis-inhibiting protein or polypeptide.

52. (New) The nucleic acid of claim 51, wherein said angiogenesis-inhibiting protein or polypeptide is selected from angiostatin, endostatin, and peptide fragments thereof.

53. (New) The nucleic acid of claim 28, 49 or 50, wherein the heterologous peptide sequence binds to a cell surface receptor protein.

54. (New) The nucleic acid of claim 53, wherein the receptor protein is a G-protein coupled receptor.

55. (New) The nucleic acid of claim 53, wherein the receptor protein is a tyrosine kinase receptor.

56. (New) The nucleic acid of claim 53, wherein the receptor protein is a cytokine receptor.

57. (New) The nucleic acid of claim 53, wherein the receptor protein is a MIRR receptor.

58. (New) The nucleic acid of claim 53, wherein the receptor protein is an orphan receptor.

59. (New) The nucleic acid of claim 28, 49 or 50, wherein the chimeric polypeptide binds to an extracellular receptor or an ion channel.

60. (**New**) The nucleic acid of claim 59, wherein the chimeric polypeptide is an agonist of said receptor or ion channel.

61. (**New**) The nucleic acid of claim 59, wherein the chimeric polypeptide is an antagonist of said receptor or ion channel.

62. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the chimeric polypeptide induces apoptosis.

63. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the chimeric polypeptide modulates cell proliferation.

64. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the chimeric polypeptide modulates differentiation of cell types.

65. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the heterologous peptide sequence comprises between 4 and 400 residues.

66. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the heterologous peptide sequence comprises between 4 and 200 residues.

67. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the heterologous peptide sequence comprises between 4 and 100 residues.

68. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the heterologous peptide sequence comprises between 4 and 20 residues.

69. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the tertiary structure of the chimeric polypeptide is similar to the tertiary structure of native SA.

70. (**New**) The nucleic acid of claim 28, wherein the inserted peptide sequence replaces a portion of native SA sequence.

71. (**New**) The nucleic acid of claim 70, wherein the inserted peptide sequence and the replaced portion of native SA sequence are of unequal length.

72. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the half-life of the polypeptide in the blood is no less than 14 days. 3

73. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the half-life of the polypeptide in the blood is no less than 10 days. 3

74. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the half-life of the polypeptide in the blood is no less than 50% of the half-life of native SA. 3

75. (**New**) A nucleic acid encoding a chimeric polypeptide comprising serum albumin (SA) having at least two biologically active heterologous peptide sequences inserted therein, wherein at least one biologically active heterologous peptide sequence is inserted (i) between an N-terminal SA sequence ending in one of residues 359-368 and a C-terminal SA sequence beginning from one of residues 361-370; or (ii) between an N-terminal SA sequence ending in one of residues 449-462 and a C-terminal SA sequence beginning from one of residues 451-464; wherein the N- and C-terminal sequences do not include overlapping portions of the regions 360-369 and 450-463.

76. (**New**) The nucleic acid of claim 75, wherein the heterologous peptide sequences are identical.

77. (**New**) The nucleic acid of claim 75, wherein the heterologous peptide sequences comprise distinct sequences of a protein.

78. (**New**) The nucleic acid of claim 75, wherein the heterologous peptide sequences comprise sequences from at least two different proteins.

79. (**New**) The nucleic acid of claim 28, 49 or 50, wherein the biologically active heterologous peptide is the myc epitope or the RGD peptide. 3

The claims presented above incorporate changes as indicated by the marked-up versions below.

28. (**Amended**) A nucleic acid encoding [the] a chimeric polypeptide [of claim 1, 2, or 3] comprising serum albumin protein (SA) having a biologically active heterologous peptide

sequence inserted into at least one region selected from residues 360-369 and residues 450-463, optionally replacing one or more residues of the region into which it is inserted.

29. (**Amended**) A delivery vector comprising the nucleic acid of claim 28, 49, or 50.

31. (**Amended**) The delivery vector of claim 30, wherein said virus or retrovirus is selected from [the group consisting of] adenoviruses, adeno-associated viruses, herpes simplex viruses, human immunodeficiency viruses, or vaccinia viruses.

33. (**Amended**) The transfected cells of claim 32, wherein the cells are selected from [the group consisting of]blood cells, skeletal muscle cells, stem cells, skin cells, liver cells, secretory gland cells, hematopoietic cells, [and]or marrow cells.

34. (**Amended**) A pharmaceutical preparation comprising a pharmaceutically acceptable excipient and the chimeric polypeptide encoded by the nucleic acid of claim [1, 2, or 3]28, 49, or 50.

4[7]8. (**Amended**) A method for modulating one or more of cell proliferation, cell differentiation, and cell death in an organism, comprising:

(i) providing a delivery vector comprising genetic material which encodes the chimeric polypeptide of claim 1, 2, or 3; and

(ii) introducing said vector into target cells *in vivo*, under conditions sufficient to induce said target cells to express said polypeptide.

REMARKS

In reply to the outstanding Restriction Requirement, mailed October 2, 2001, in connection with the above application, Applicants hereby elect Group II with traverse, based on the reasons which follow. The time period for response has been extended to January 2, 2002, by the accompanying petition for a two-month extension of time.

Applicants have amended claims 28, 29, 34, and 48, and have added new claims 49-83. Applicants submit that these claims (except claim 48) all belong to Group II. Claims 49 and 50

result from re-writing claim 28 into independent form, and are supported by original claims 1-3 and 28, as well as the specification from page 35, 3rd full paragraph to page 36, 2nd paragraph.

Applicants also note that the Office Action has accidentally failed to consider the original claims 47 and 48 (both mistakenly numbered "47").

Applicants submit that all the new claims belong to the elected Group II, directed to nucleic acids encoding polypeptides of Groups I, V and VI. Accordingly, Applicants submit that the claims of Groups I, V, and VI are so closely related to the elected claims of Group II that there would be no significant additional burden on the Examiner to search Groups I, II, V, and VI simultaneously. Pursuant to MPEP 803, a restriction is improper if there is no serious burden on the Examiner to search all Groups simultaneously. Therefore, reconsideration and withdrawal of the restriction requirement between Groups I, II, V, and VI are respectfully requested.

Similarly, Groups III and IV together with the non-considered claims 47-48 have only 6 claims directed to use of products claimed in Groups I, II, V and VI. Applicants submit that there is no significant additional burden on the Examiner to search these Groups with the others, and therefore reconsideration and withdrawal of the restriction requirement are respectfully requested.

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

Date: December 20, 2001

Yu Lu, Ph.D.
Reg. No. P-50,306

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Docketing Specialist
Ropes & Gray
One International Place
Boston, MA 02110
Phone: 617-951-7000
Fax: 617-951-7050

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FILE LAST UPDATED: 18 Mar 2002  (20020318/ED)

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Numbers with the P indicator executed between 12/27/01 and 1/23/02 may
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=> d que l28; d que l29; d que l30; d que l39

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L11        9523 SEA FILE=CAPLUS ABB=ON  TRANSFECT?/OBI
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L16       18816 SEA FILE=CAPLUS ABB=ON  BONE MARROW/CT
L17        5269 SEA FILE=CAPLUS ABB=ON  GLAND+OLD/CT
L18       13194 SEA FILE=CAPLUS ABB=ON  HEMATOPOIETIC PRECURSOR CELL/CT
L19      266039 SEA FILE=CAPLUS ABB=ON  LIVER/CT
L20       60968 SEA FILE=CAPLUS ABB=ON  SKIN/CT
L21       96254 SEA FILE=CAPLUS ABB=ON  MUSCLE+OLD/CT
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                L19 OR L20 OR L21))(L)L11
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L24       22228 SEA FILE=CAPLUS ABB=ON  HERPES?/OBI
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=> s l28 or l29 or l30 or l39

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=> fil wpids; d que l49

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L49            5 SEA FILE=WPIDS ABB=ON  L47 AND (L42 OR L43) AND L44


=> fil biosis

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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
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RECORDS LAST ADDED: 13 March 2002 (20020313/ED)

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L72	3	SEA FILE=BIOSIS ABB=ON	L65 AND L68 AND L71

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L74	5	SEA FILE=BIOSIS ABB=ON	L73 AND L65
L75	1	SEA FILE=BIOSIS ABB=ON	L74 AND MORI

L148 4 L72 OR L75

=> fil biotechds; d que l90

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L81	32966	SEA FILE=BIOTECHDS ABB=ON	?VIRUS? OR ?VIRAL OR ?VIRIDA?
L82	4026	SEA FILE=BIOTECHDS ABB=ON	RETROVIR? OR HERPES?
L83	9740	SEA FILE=BIOTECHDS ABB=ON	TRANSFECT?
L84	40394	SEA FILE=BIOTECHDS ABB=ON	TRANSFORM?
L85	569	SEA FILE=BIOTECHDS ABB=ON	L84(W)GROWTH FACTOR#
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=> fil embase; d que l143; d que l145

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L123       10564 SEA FILE=EMBASE ABB=ON  HYBRID PROTEIN/CT
L124        2196 SEA FILE=EMBASE ABB=ON  CHIMERIC PROTEIN/CT
L143           6 SEA FILE=EMBASE ABB=ON  L122 AND (L123 OR L124)



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L128       12670 SEA FILE=EMBASE ABB=ON  ADENOVIRUS+NT/CT
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L131       43010 SEA FILE=EMBASE ABB=ON  HUMAN IMMUNODEFICIENCY VIRUS+NT/CT
L132         382 SEA FILE=EMBASE ABB=ON  VACCINIA/CT
L145           0 SEA FILE=EMBASE ABB=ON  L125 AND L122 AND ((L128 OR L129 OR
                 L130 OR L131 OR L132))


=> fil medl

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 On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

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 MEDLINE is now updated 4 times per week. A new current-awareness alert
 frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
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 The OLDMEDLINE file segment now contains data from 1958 through 1965.
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 Left, right, and simultaneous left and right truncation are available in the
 Basic Index. See HELP SFIELDS for details.

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 SUBSTANCE IDENTIFICATION.

=> d que l113; d que l115; d que l121

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Subheading GE = genetics

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=> dup rem l149,l147,l148,l143,l90,l49
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PROCESSING COMPLETED FOR L90
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                 ANSWERS '5-15' FROM FILE CAPLUS
                 ANSWERS '16-19' FROM FILE BIOSIS
                 ANSWERS '20-25' FROM FILE EMBASE
                 ANSWERS '26-27' FROM FILE BIOTECHDS
                 ANSWERS '28-31' FROM FILE WPIDS

=> d ibib ab 1-31; fil hom
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L150 ANSWER 1 OF 31 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 94297617 MEDLINE
DOCUMENT NUMBER: 94297617 PubMed ID: 8025593
TITLE: Ectopic expression of beta-lactoglobulin/human serum albumin fusion genes in transgenic mice: hormonal regulation and in situ localization.
AUTHOR: Barash I; Faerman A; Ratovitsky T; Puzis R; Nathan M; Hurwitz D R; Shani M
CORPORATE SOURCE: Institute of Animal Science, Volcani Center, Bet Dagan, Israel.
SOURCE: TRANSGENIC RESEARCH, (1994 May) 3 (3) 141-51.
Journal code: BRX; 9209120. ISSN: 0962-8819.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940818
Last Updated on STN: 19940818
Entered Medline: 19940811

AB We produced transgenic mice carrying the native sheep beta-lactoglobulin (BLG) or fusion genes composed of the BLG promoter and human serum albumin (HSA) minigenes. BLG was expressed exclusively in the mammary glands of the virgin and lactating transgenic mice evaluated. In contrast, transgenic females carrying the BLG/HSA fusion constructs also expressed the HSA RNA ectopically in skeletal muscle, kidney, brain, spleen, salivary gland and skin. Ectopic expression of HSA RNA was detected only in strains that express the transgene in the mammary gland. There was no obvious correlation between the level of the HSA RNA expressed in the mammary gland and that found ectopically. In three transgenic strains analysed, the expression of HSA RNA in kidney and skeletal muscle increased during pregnancy and lactation, whereas in the brain HSA expression decreased during lactation in one of the strains. HSA protein was synthesized in skeletal muscle and skin of strain #23 and its level was higher in lactating mice compared with virgin mice. Expression of HSA was also analysed in males and was found to be more stringently controlled than in females of the same strains. In situ hybridization analyses localized the expressed transgene in the skin, kidney, brain and salivary glands of various transgenic strains. Distinct strain-specific and cell-type specific HSA expression patterns were observed in the skin. This is in contrast to the exclusive expression of the HSA transgene in epithelial cells surrounding the alveoli of the mammary gland. Taken together, these results suggest that the absence of sufficient mammary-specific regulatory elements in the BLG promoter sequences and/or the juxtaposition of the BLG promoter with the HSA coding sequences leads to novel tissue- and cell-specific expression in ectopic tissues of transgenic mice.

L150 ANSWER 2 OF 31 MEDLINE
ACCESSION NUMBER: 97275135 MEDLINE
DOCUMENT NUMBER: 97275135 PubMed ID: 9129029
TITLE: Potent antithrombin activity and delayed clearance from the circulation characterize recombinant hirudin genetically fused to albumin.
AUTHOR: Syed S; Schuyler P D; Kulczycky M; Sheffield W P
CORPORATE SOURCE: Department of Pathology, McMaster University, Hamilton, Ontario, Canada.
SOURCE: BLOOD, (1997 May 1) 89 (9) 3243-52.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

OTHER SOURCE: GENBANK-U18344
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19990129
Entered Medline: 19970603

AB In this study we sought to extend the plasma half-life while maintaining the potent antithrombin activity of hirudin. We hypothesized that gene fusion of hirudin to albumin would result in the expression of a slowly cleared hirudin molecule. A hirudin variant 3 (HV3) cDNA was obtained by gene synthesis, while a 1,996-bp full-length rabbit serum albumin (RSA) cDNA was selected from a rabbit liver cDNA library. Expression of the former in COS-1 cells conferred antithrombin activity on media conditioned by the cells, while expression of the latter resulted in the secretion of a 67-kD protein that reacted with mono-specific anti-RSA antibodies. Having shown independent expression of the two proteins, we next expressed two fusion proteins: HV3 linked via its C-terminus to albumin (HLA), and HV3 linked via its N-terminus to albumin (ALH). The former, but not the latter, inhibited both the amidolytic and fibrinogenolytic activities of thrombin. HLA also retained the dye-binding characteristics of RSA, as judged by Affi-Gel Blue chromatography. Highly similar concentrations of either commercial HV1 (40 nmol/L) or HLA (30 nmol/L) were required to halve the initial rate of thrombin reaction with chromogenic substrate S2238, suggesting the retention of high-affinity inhibition of thrombin by the fusion protein. An His-tagged form of HLA was purified by Ni2+-chelate affinity and heparin-Sepharose chromatography. The purified, radioiodinated protein was injected into rabbits, and demonstrated a catabolic half-life of 4.60 +/- 0.16 days. This represents an extension of hirudin half-life in vivo of greater than two orders of magnitude; gel analysis of HLA(H)6 recovered from rabbits showed that it circulated in intact form. Our results provide a rationale for future testing of the biological effects of HLA, and support our initial hypothesis.

L150 ANSWER 3 OF 31 MEDLINE
ACCESSION NUMBER: 92179291 MEDLINE
DOCUMENT NUMBER: 92179291 PubMed ID: 1542690
TITLE: Design of yeast-secreted albumin derivatives for human therapy: biological and antiviral properties of a serum albumin-CD4 genetic conjugate.
AUTHOR: Yeh P; Landais D; Lemaitre M; Maury I; Crenne J Y; Becquart J; Murry-Brelier A; Boucher F; Montay G; Fleer R; +
CORPORATE SOURCE: Rhone-Poulenc Rorer, Centre de Recherche de Vitry-Alfortville, Vitry, France.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 Mar 1) 89 (5) 1904-8.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 19920424
Last Updated on STN: 19970203
Entered Medline: 19920407

AB Due to its remarkably long half-life, together with its wide in vivo distribution and its lack of enzymatic or immunological functions, human serum albumin (HSA) represents an optimal carrier for therapeutic peptides/proteins aimed at interacting with cellular or molecular components of the vascular and interstitial compartments. As an example, we designed a genetically engineered HSA-CD4 hybrid aimed at specifically blocking the entry of the human immunodeficiency virus into CD4+ cells. In contrast with CD4, HSA-CD4 is correctly processed and efficiently secreted by Kluyveromyces yeasts. In addition, its CD4 moiety exhibits binding and antiviral in vitro properties similar to those of soluble CD4. Finally,

the elimination half-life of HSA-CD4 in a rabbit experimental model is comparable to that of control HSA and 140-fold higher than that of soluble CD4. These results indicate that the genetic fusion of bioactive peptides to HSA is a plausible approach toward the design and recovery of secreted therapeutic HSA derivatives with appropriate pharmacokinetic properties.

L150 ANSWER 4 OF 31 MEDLINE
ACCESSION NUMBER: 90158113 MEDLINE
DOCUMENT NUMBER: 90158113 PubMed ID: 2482921
TITLE: Activity of a metallothionein-transthyretin fusion gene in transgenic mice. Possible effect of plasmid sequences on tissue-specific expression.
AUTHOR: Sasaki H; Nakazato M; Saraiva M J; Matsuo H; Sakaki Y
CORPORATE SOURCE: Research Laboratory for Genetic Information, Kyushu University, Fukuoka, Japan.
SOURCE: MOLECULAR BIOLOGY AND MEDICINE, (1989 Aug) 6 (4) 345-53. Journal code: MOL; 8403879. ISSN: 0735-1313.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19960129
Entered Medline: 19900320

AB Three strains of transgenic mice carrying the mouse metallothionein-I (MT) promoter fused to the human transthyretin (TTR) structural gene plus pUC plasmid sequences were investigated for expression of the fusion gene. Human TTR was inducible in the serum of at least two strains and the fusion gene mRNA was detected in several tissues of all the strains. The testis showed constitutive mRNA synthesis, while the intestine and some other tissues showed inducible expression. Unexpectedly, however, the fusion gene activity was grossly suppressed in the liver and kidney of all the strains. Available data suggest that this suppression results from the presence of the plasmid sequences. Analysis of tissue DNAs shows that the methylation status of the promoter sequences varies from strain to strain, depending on their chromosomal position, and that some CpG sites in the proximal portion of the promoter are not methylated at all in the liver and kidney of two strains. These findings suggest that the plasmid sequences suppress the MT promoter activity in some specific tissues by a mechanism that does not involve DNA methylation.

L150 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:64027 CAPLUS
DOCUMENT NUMBER: 134:110478
TITLE: Chimeric polypeptides of serum albumin containing heterologous peptide sequences, and therapeutic uses thereof
INVENTOR(S): Gyuris, Jeno; Lamphere, Lou
PATENT ASSIGNEE(S): GPC Biotech Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005826	A2	20010125	WO 2000-US19689	20000719
WO 2001005826	A3	20010802		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-144534P P 19990719

AB The invention discloses chimeric polypeptides in which a serum albumin protein has been altered to include one or more biol. active heterologous peptide sequences. The chimeric polypeptides may exhibit therapeutic activity related to the heterologous peptide sequences coupled with the improved serum half-lives derived from the serum albumin protein fragments. Heterologous peptide sequences may be chosen to promote any biol. effect, including angiogenesis inhibition, antitumor activity, and induction of apoptosis. The therapeutic effect may be achieved by direct administration of the chimeric polypeptide, or by transfecting cells with a vector including a nucleic acid encoding such a chimeric polypeptide.

L150 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:780950 CAPLUS
DOCUMENT NUMBER: 135:322687
TITLE: Albumin fusion proteins with therapeutic proteins for improved shelf-life
INVENTOR(S): Ballance, David James; Sleep, Darrell; Turner, Andrew John; Sadeghi, Homayoun; Prior, Christopher P.
PATENT ASSIGNEE(S): Principia Pharmaceutical Corporation, USA; Delta Biotechnology Limited
SOURCE: PCT Int. Appl., 338 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079271	A1	20011025	WO 2001-US12009	20010412

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-229358P P 20000412
US 2000-199384P P 20000425
US 2000-256931P P 20001221

AB The present invention encompasses fusion proteins of albumin with various therapeutic proteins, and in particular interferon .alpha. and various blood coagulation factors. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in soln., in vitro and/or in vivo, by genetically or chem. fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of albumin fusion proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors contg. these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the

albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the albumin fusion proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth hormone with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37.degree., whereas recombinant human growth hormone used as control lost its biol. activity in the first week. Although the potency of the albumin fusion proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:936090 CAPLUS
DOCUMENT NUMBER: 136:58776
TITLE: Chimeric polypeptides of serum albumin and uses related thereto
INVENTOR(S): Gyuris, Jeno; Lamphere, Lou
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 619,285.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001056075	A1	20011227	US 2001-764918	20010118

PRIORITY APPLN. INFO.: US 1999-144534P P 19990719
US 2000-619285 A2 20000719

AB The present invention relates to chimeric polypeptides in which a serum albumin protein has been altered to include one or more biol. active heterologous peptide sequences. The chimeric polypeptides may exhibit therapeutic activity related to the heterologous peptide sequences coupled with the improved serum half-lives derived from the serum albumin protein fragments. Heterologous peptide sequences may be chosen to promote any biol. effect, including angiogenesis inhibition, antitumor activity, and induction of apoptosis. The therapeutic effect may be achieved by direct administration of the chimeric polypeptide, or by transfecting cells with a vector including a nucleic acid encoding such a chimeric polypeptide.

L150 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:390425 CAPLUS
DOCUMENT NUMBER: 131:43579
TITLE: Recombinant **nodavirus** compositions and methods
INVENTOR(S): Hall, Stephen G.
PATENT ASSIGNEE(S): Pentamer Pharmaceuticals, USA; The Scripps Research Institute
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929723	A1	19990617	WO 1998-US25922	19981207
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6171591	B1	20010109	US 1997-986659	19971208
AU 9917146	A1	19990628	AU 1999-17146	19981207
EP 1037917	A1	20000927	EP 1998-961962	19981207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9813416	A	20011016	BR 1998-13416	19981207
JP 2001525422	T2	20011211	JP 2000-524314	19981207

PRIORITY APPLN. INFO.: US 1997-986659 A 19971208
WO 1998-US25922 W 19981207

AB Recombinant **nodavirus** related compns. are disclosed. These compns. include chimeric proteins in which a **nodavirus** capsid protein is present together with a heterologous peptide segment. The heterologous peptide includes at least one cell-specific targeting sequence, such as a B cell epitope, a T cell epitope, or a sequence specific for another cell type, such as a hepatocyte. The chimeric proteins can be assembled to form chimeric **virus**-like particles. The chimeric **virus**-like particles are useful in therapeutic applications, such as vaccines and gene-delivery vectors, and in diagnostic applications, such as kits for the testing of body tissue or fluid samples. Methods for the use of recombinant **nodavirus** related compns. in therapeutic and diagnostic applications are also described.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:101678 CAPLUS
DOCUMENT NUMBER: 133:63719
TITLE: In-vivo delivery of therapeutic proteins by genetically-modified cells: comparison of organoids and human serum albumin alginate-coated beads
AUTHOR(S): Shinya, E.; Dervillez, X.; Edwards-Levy, F.; Duret, V.; Brisson, E.; Ylisastigui, L.; Levy, M. C.; Cohen, J. H. M.; Klatzmann, D.
CORPORATE SOURCE: Laboratoire de biologie et therapeutique des pathologies immunitaires, UPMC/CNRS ESA 7087, CERVI, Hopital de la Pitie-Salpetriere, 83, boulevard de l'Hopital, Paris, 75651/13, Fr.
SOURCE: Biomed. Pharmacother. (1999), 53(10), 471-483
CODEN: BIPHEX; ISSN: 0753-3322
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have designed a self-assembling multimeric sol. CD4 mol. by inserting the C-terminal fragment of the alpha chain of human C4-binding protein (C4bp.alpha.) at the C-terminal end of human sol. CD4 genes. This CD4-C4bp.alpha. fusion protein (sMulti-CD4) and two other ref. mols., a

fusion protein of human serum albumin (HSA) and the first two domains of CD4 (HSA-CD4) and monomeric sol. CD4 (sMono-CD4), were delivered in vivo by genetically modified 293 cells. These cells were implanted in mice as organoids and also encapsulated in HSA alginate-coated beads. SMulti-CD4 showed an apparent mol. wt. of about 300-350 kDa, in accordance with a possible heptamer formula. SMulti-CD4 produced either in cell culture or in vivo in mice appeared to be a better in-vitro inhibitor of HIV infection than sMono-CD4. Plasma levels of sMulti-CD4, HSA-CD4, and sMono-CD4 reached approx. 2300, 2700, and 170 ng/mL, resp., 13 wk after in-vivo organoid implantation, which had formed tumors at that time. This suggests that the plasma half-life of sMulti-CD4 is much longer than that of sMono-CD4. The 293 xenogeneic cells encapsulated in HSA/alginate-coated beads remained alive and kept secreting sMono-CD4 or HSA-CD4 continuously at significant levels for 18 wk in nude mice, without tumor formation. When implanted in immunocompetent Balb/c mice, they were rejected two to three weeks after implantation. In contrast, encapsulated BL4 hybridoma cells remained alive and kept secreting BL4 anti-CD4 mAb for at least four weeks in Balb/c mice. These results suggest the clin. potential of the C4bp-multimerizing system, which could improve both the biol. activity and the poor in-vivo pharmacokinetic performance of a monomeric functional protein like sol. CD4. These data also show that a systemic delivery of therapeutic proteins, including Igs, can be obtained by the in-vivo implantation of engineered allogeneic cells encapsulated in HSA/alginate-coated beads.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L150 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:724599 CAPLUS
DOCUMENT NUMBER: 128:21674
TITLE: Efficient production of active TNF-.alpha. by albumin signal peptide
AUTHOR(S): Maeda, Yuu; Soda, Mariko; Ito, Keizo; Sato, Kenzo
CORPORATE SOURCE: Department of Molecular Biology, School of Life Sciences, Faculty of Medicine, Tottori University, Yonago, 683, Japan
SOURCE: Biochem. Mol. Biol. Int. (1997), 42(4), 825-832
CODEN: BMBIES; ISSN: 1039-9712
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TNF-.alpha. is initially synthesized as a membrane-anchored precursor protein and processed proteolytically by a matrix metalloproteinase (MMP)-like enzyme. In order to establish an efficient expression system of TNF-.alpha. in mammalian cells without involvement of the extracellular enzyme, an expression plasmid (pCN-alb-TNF) was constructed with a signal sequence of the rat albumin gene as a module for secretion. The highest level of prodn. of TNF-.alpha. was obsd. in the clone CT-3 by SDS-PAGE and Western blot anal. Biol. activity of the secretion was revealed by repression of catalase gene expression in hepatoma cells and cytotoxicity to L929 cells. Attachment of the signal peptide to mature form resulted in the enhancement of prodn. of the cytokine.

L150 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:363692 CAPLUS
DOCUMENT NUMBER: 125:48833
TITLE: Systemic and portal vein delivery of human kallikrein gene reduces blood pressure in hypertensive rats
AUTHOR(S): Chao, Julie; Jin, Lan; Chen, Li-Mei; Chen, Vincent C.; Chao, Lee
CORPORATE SOURCE: Department Biochemistry and Molecular Biology, Medical University South Carolina, Charleston, SC, 29425-2211, USA

Searched by Barb O'Bryen, STIC 308-4291

SOURCE: Hum. Gene Ther. (1996), 7(8), 901-911
CODEN: HGTHE3; ISSN: 1043-0342
DOCUMENT TYPE: Journal
LANGUAGE: English

AB There is an inverse correlation between systemic blood pressure and urinary kallikrein levels in humans and hypertensive animal models, suggesting that the tissue kallikrein-kinin system plays an important role in blood pressure regulation. In this study, we explored the potential of human kallikrein gene delivery on blood pressure redn. in spontaneously hypertensive rats (SHR). The human tissue kallikrein gene or cDNA was placed under the control of following promoters: the metallothionein gene metal response-element (MRE-pHK), albumin gene (ALB-pHK), Rous sarcoma **virus** 3' long terminal repeat (LTR) (RSV-cHK), and **cytomegalovirus** (CMV-cHK). A single injection of these kallikrein DNAs results in a significant redn. of blood pressure in SHR, which lasts for 5-6 wk. Systemic delivery of CMV-cHK, RSV-cHK, and MRE-pHK has a greater effect on blood pressure redn. than ALB-pHK, whereas intraportal vein gene delivery of ALB-pHK is more effective than the other kallikrein DNA constructs. The degree of blood pressure redn. depends on the amt. of administered DNA and the age of the animals. Redn. of blood pressure was obsd. in adult, but not young, SHR. The expression of human tissue kallikrein in rats was identified by an ELISA that is specific for human tissue kallikrein. No antibodies to either human tissue kallikrein or its DNA were detected in rat sera after somatic gene delivery. These results show that somatic gene delivery of human tissue kallikrein causes a lowering effect of systolic blood pressure in genetically hypertensive rats and provide valuable information for kallikrein gene therapy in the treatment of hypertension.

L150 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:136528 CAPLUS
DOCUMENT NUMBER: 124:222801
TITLE: Regulated expression of artificial chimeric genes contained in **retroviral** vectors: implications for **virus**-directed enzyme prodrug therapy (VDEPT) and other gene therapy applications
AUTHOR(S): Huber, Brian E.; Richards, Cynthia A.
CORPORATE SOURCE: Div. Cell Biol., Wellcome Res. Lab., Research Triangle Park, NC, USA
SOURCE: J. Drug Targeting (1996), 3(5), 349-56
CODEN: JDTAEH; ISSN: 1061-186X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Replication-defective **retroviral** vectors were created that contained chimeric genes composed of either the albumin (ALB) or the alpha-fetoprotein (AFP) transcriptional regulatory sequences linked to the coding domain of the thymidine kinase gene from Varicella zoster **virus** (VZV TK). These **viruses** were used to infect the human hepatoblastoma cell line, HepG2. Subsequent to infection, the infected cells were single-cell cloned. The level of expression of VZV TK from the chimeric genes correlated with the level of endogenous expression of ALB or AFP in most clones, indicating that the transcription of the chimeric VZV TK gene is controlled in a similar manner to the endogenous ALB or ALP genes, and that sites of **viral** integration are less important to overall gene expression. Most importantly, as the expression of the endogenous ALB gene was modified, so was expression of VZV TK from the ALB/VZV TK chimeric gene. This demonstrates that **retroviruses** can deliver a chimeric gene contg. tissue-specific transcriptional regulatory sequences that can respond to endogenous cell regulatory signals resulting in regulated gene expression.

L150 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:591573 CAPLUS
DOCUMENT NUMBER: 122:310285
TITLE: Establishment of hepatoma cell line for neoplasm inhibitor screening
INVENTOR(S): Shiho, Osamu; Tojo, Hideaki; Nakada, Mitsugi
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07079773	A2	19950328	JP 1994-166647	19940719
PRIORITY APPLN. INFO.:			JP 1993-179402	19930720

AB Disclosed is the establishment of a cell line by transferring SV40-T gene and albumin promoter gene into mouse hepatoma. The hepatoma cell line is useful for screening anti-tumor agents. In example, fusion gene encoding mouse albumin promoter and SV40-T was transferred to mouse hepatoma and grown in s.c. tissues of mice.

L150 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:123004 CAPLUS
DOCUMENT NUMBER: 116:123004
TITLE: Arrest of embryo development in Brassica napus mediated by modified Pseudomonas aeruginosa exotoxin A
AUTHOR(S): Koning, Ann; Jones, Aubrey; Fillatti, JoAnne J.; Comai, Luca; Lassner, Michael W.
CORPORATE SOURCE: Calgene Inc., Davis, CA, 95616, USA
SOURCE: Plant Mol. Biol. (1992), 18(2), 247-58
CODEN: PMBIDB; ISSN: 0167-4412
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intracellularly expressed cytotoxins are useful tools both to study the action of plant regulatory sequences in transgenic plants and to modify plant phenotype. A low mammalian toxicity deriv. of P. aeruginosa exotoxin A was engineered for intracellular expression in plant cells by fusing the ADP ribosylating domain of the exotoxin gene to plant regulatory sequences. The efficacy of exotoxin A on plant cells was demonstrated by transient expression of the modified exotoxin gene in tobacco protoplasts; the exotoxin gene inhibited the expression of a co-electroporated .beta.-glucuronidase gene. An exotoxin with an introduced frameshift mutation was also effective at inhibiting .beta.-glucuronidase expression in the transient assay; the activity of the frameshifted gene was presumably a result of frameshifting during translation or initiation of translation at a codon other than AUG. When fused to napin regulatory sequences, the exotoxin gene specifically arrested embryo development in the seeds of transgenic B. napus plants concomitant with the onset of napin expression. The napin/exotoxin chimeric gene did not have the same pattern of expression in tobacco as in B. napus; in addn. to exhibiting an inhibition of seed development, the transgenic tobacco plants were male-sterile.

L150 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:571187 CAPLUS
DOCUMENT NUMBER: 111:171187
TITLE: Transport of proteins to the plant vacuole is not by bulk flow through the secretory system, and requires positive sorting information
AUTHOR(S): Dorel, Corinne; Voelker, Toni A.; Herman, Eliot M.; Chrispeels, Maarten J.

Searched by Barb O'Bryen, STIC 308-4291

CORPORATE SOURCE: Cent. Mol. Genet., Univ. California, San Diego, CA, 92093-0116, USA
SOURCE: J. Cell Biol. (1989), 108(2), 327-37
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plant cells, like other eukaryotic cells, use the secretory pathway to target proteins to the vacuolar/lysosomal compartment and to the extracellular space. To det. whether the presence of a hydrophobic signal peptide would result in the transport of a reporter protein to vacuoles by bulk flow, a chimeric gene was expressed in transgenic tobacco. The chimeric gene, Phalb, used for this study consists of the 1188-base pair 5' upstream sequence and the hydrophobic signal sequence of a vacuolar seed protein phytohemagglutinin, and the coding sequence of a cytosolic seed albumin (PA2). The chimeric protein PHALB cross-reacted with antibodies to PA2 and was found in the seeds of the transgenic plants (.apprx.0.7% of total protein), but not in the leaves, roots, or flowers. Immunoblot analyses of seed exts. revealed 4 glycosylated polypeptides ranging in mol. wt. from 29,000 to 32,000. The 4 polypeptides are glycoforms of a single polypeptide of Mr 27,000, and the heterogeneity is due to the presence of high mannose and endoglycosidase H-resistant glycans. The PHALB products reacted with an antiserum specific for complex plant glycans indicating that the glycans had been modified in the Golgi app. Subcellular fractionation of glycerol exts. of mature seeds showed that only small amts. of PHALB accumulated in the protein storage vacuoles of the tobacco seeds. In homogenates made in an isotonic medium, very little PHALB was assocd. with the organelle fraction contg. the endoplasmic reticulum and Golgi app.; most of it was in the sol. fraction. Apparently, PHALB passed through the Golgi app., but did not arrive in the vacuoles. Transport to vacuoles is not by a bulk-flow mechanism, once proteins have entered the secretory system, and requires information beyond that provided by a hydrophobic signal peptide.

L150 ANSWER 16 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:137093 BIOSIS
DOCUMENT NUMBER: PREV200200137093
TITLE: Human serum albumin production in silkworm Bombyx **mori** fourth instar larvae.
AUTHOR(S): Kozuma, Kazuya; Kato, Masao; Hamano, Kunikatsu (1)
CORPORATE SOURCE: (1) Department of Biological Production, Faculty of Agriculture, Tokyo University of Agriculture and Technology, Saiwaicho 3-5-8, Fuchu, Tokyo, 183-8509: hamano@cc.tuat.ac.jp Japan
SOURCE: Journal of Insect Biotechnology and Sericology, (October, 2001) Vol. 70, No. 3, pp. 183-188. print.
DOCUMENT TYPE: Article
LANGUAGE: English

AB **Recombinant** human serum **albumin** (rHSA) was produced using the **recombinant** Bombyx **mori** **nucleopolyhedrovirus** (rNPV) **vector** in silkworm larvae. rHSA was purified by ion exchange chromatography, affinity chromatography, and gel filtration chromatography from the whole-body homogenate of infected 4th instar larvae. No impurities were detected in the purified rHSA by reverse-phase chromatography and SDS-polyacrylamide gel electrophoresis. We obtained 3.48 mg of mature rHSA (removed preprosequence) from 24 4th instar larvae on day 4 postinfection (1X102 PFU/larva). These results suggest that efficient rHSA mass production is possible using the rNPV vector and B. **mori** 4th instar larvae.

L150 ANSWER 17 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:463205 BIOSIS
DOCUMENT NUMBER: PREV200100463205
TITLE: Development of expression systems for the production of

recombinant human serum **albumin** using the MOX promoter in Hansenula polymorpha DL-1.

AUTHOR(S): Kang, Hyun Ah; Kang, Whankoo; Hong, Won-Kyuong; Kim, Moo Woong; Kim, Jeong-Yoon; Sohn, Jung-Hoon; Choi, Eui-Sung; Choe, Keun-Bum; Rhee, Sang Ki (1)
CORPORATE SOURCE: (1) Korea Research Institute of Bioscience and Biotechnology, Taejon, 305-600: rheesk@mail.kribb.re.kr South Korea
SOURCE: Biotechnology and Bioengineering, (September, 2001) Vol. 76, No. 2, pp. 175-185. print.
ISSN: 0006-3592.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To optimize the secretory expression of **recombinant** human serum **albumin** (HSA) under the control of methanol oxidase (MOX) promoter in the methylotrophic yeast Hansenula polymorpha DL-1, we analyzed several parameters affecting the expression of HSA from the MOX promoter. Removal of the 5'-untranslated region derived from HSA cDNA in the expression cassette led to at least a fivefold improvement of HSA expression efficiency at the translational level. With the optimized expression cassette, the gene dosage effect on HSA expression was abolished and thus, a single copy of the expression vector integrated into the MOX locus became sufficient for the maximal expression of HSA. Northern blot analysis revealed that the levels of HSA transcript did not increase any further upon increasing copy number. The mox-disrupted (moxDELTA) **transformant** was constructed, in which the genomic MOX gene was transplaced with the HSA expression cassette, to examine the effect of the methanol oxidase-deficient phenotype of the host on HSA expression. The moxD **transformant** showed higher levels of HSA production in shake-flask cultures than the MOX wild-type **transformant**, especially at low concentrations of methanol and a twofold higher specific HSA production rate in fed-batch fermentation with an abrupt induction mode. The native prepro signal sequence of HSA secreted in H. polymorpha was correctly processed and the mature recombinant protein had a pl value identical to that of the authentic HSA. Our results suggest that the H. polymorpha expression systems developed in this study are suitable for large-scale production of **recombinant albumin**.

L150 ANSWER 18 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:191050 BIOSIS
DOCUMENT NUMBER: PREV200000191050
TITLE: Transgenic mouse models in carcinogenesis research and testing.
AUTHOR(S): Thorgeirsson, Snorri S. (1); Factor, Valentina M.; Snyderwine, Elizabeth G.
CORPORATE SOURCE: (1) Laboratory of Experimental Carcinogenesis, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, 37 Convent Drive, Room 3C28, Building 37, Bethesda, MD, 20892-4255 USA
SOURCE: Toxicology Letters (Shannon), (March 15, 2000) No. 112-113, pp. 553-555.
ISSN: 0378-4274.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Double transgenic mice bearing **fusion** genes consisting of mouse **albumin** enhancer/promoter-mouse c-myc cDNA and mouse metallothionein 1 promoter-human TGF-alpha cDNA were generated to investigate the interaction of these genes in hepatic oncogenesis and to provide a general paradigm for characterizing both the interaction of nuclear oncogenes and growth factors in tumorigenesis. In addition, these mice provide an experimental model to test how environmental chemicals

might interact with the c-myc and TGF-alpha transgenes during the neoplastic process. We show experimental evidence that co-expression of TGF-alpha and c-myc transgenes in mouse liver promotes overproduction of ROS and thus creates an oxidative stress environment. This phenomenon may account for the massive DNA damage and acceleration of hepatocarcinogenesis observed in the TGF-alpha/c-myc mouse model. Also, the role of mutagenesis in hepatocarcinogenesis induced by 2-amino-3,8-dimethylimidazo(4,5-f)-quinoxaline (MeIQx) was demonstrated in C57BL/lacZ (MutaTM Mice) and double transgenic c-myc/lacZ mice that carry the lacZ mutation reporter gene. The MeLQx hepatocarcinogenicity was associated with an increase in in vivo mutagenicity as scored by mutations in the lacZ reporter gene. These results suggest that transgenic mouse models may provide important tools for testing both the carcinogenic potential of environmental chemicals and the interaction/cooperation of these compounds with specific genes during the neoplastic process.

L150 ANSWER 19 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:48618 BIOSIS
DOCUMENT NUMBER: BA93:28593
TITLE: HIGH-LEVEL SEED-SPECIFIC EXPRESSION OF FOREIGN CODING SEQUENCES IN BRASSICA-NAPUS.
AUTHOR(S): STAYTON M; HARPSTER M; BROSIO P; DUNSMUIR P
CORPORATE SOURCE: DNA PLANT TECHNOLOGY INC., 6701 SAN PABLO AVENUE, OAKLAND, CALIF. 94608, USA.
SOURCE: AUST J PLANT PHYSIOL, (1991) 18 (5), 507-518.
CODEN: AJPPCH. ISSN: 0310-7841.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The napin seed storage proteins of oilseed rape (Brassica napus) are encoded by a multigene family of a least 16 members. We have isolated five independent napin genes and five napin cDNAs from a rapid cycling line of B. napus (CrGC45). Two of the isolated genomic fragments, G1 and G2, were introduced into tobacco, and napin gene expression was analyzed in the developing seeds. Both genes are expressed during the maturation phase of **transformed** tobacco seeds as judged by the accumulation of napin RNA in immature embryos. The genes appear to utilise the same transcription start site in tobacco as in Brassica, but are expressed at 20-50-fold lower levels in the heterologous host plant. The G1 and G2 promoter regions and 3' flanking regions were also fused to two foreign coding sequences: the chloramphenicol acetyl transferase (CAT) coding sequence and the pea seed 2S **albumin** (PSA) coding sequence, and these **chimeric** genes were introduced into B. napus and tobacco. Upon introduction into tobacco, only the PSA mRNA accumulated to a measureable extent. In transgenic rapeseed plants, PSA RNA accumulated to high levels, but CAT RNA was present only a low concentrations. The results demonstrate that high level expression of foreign coding sequences is possible in developing seeds of B. napus and the differential mRNA stability may contribute significantly to the level of foreign transcripts which can be observed in genetically engineered rapeseed.

L150 ANSWER 20 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001121801 EMBASE
TITLE: Screening of a unique lectin from 16 cultivable mushrooms with hybrid glycoprotein and neoproteoglycan probes and purification of a novel N-acetylglucosamine-specific lectin from Oudemansiella platyphylla fruiting body.
AUTHOR: Matsumoto H.; Natsume A.; Ueda H.; Saitoh T.; Ogawa H.
CORPORATE SOURCE: H. Ogawa, Grad. Sch. of Humanities and Sci., Course of Advanced Biosciences, Ochanomizu University, 2-1-1 Otsuka, Bunkyo-ku, Tokyo 112-8610, Japan. hogawa@cc.ocha.ac.jp
SOURCE: Biochimica et Biophysica Acta - General Subjects, (3 Apr 2001) 1526/1 (37-43).
Refs: 23

ISSN: 0304-4165 CODEN: BBGSB3
PUBLISHER IDENT.: S 0304-4165(01)00094-0
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hybrid glycoprotein and neoproteoglycan probes were prepared by coupling various glycoproteins or polysaccharides to peroxidase or biotinyl bovine serum albumin, respectively. Lectins recognizable by the neoglycoconjugate probes were extracted from 16 cultivable mushrooms. Dot-blot assay revealed five extracts to be reactive with only hybrid glycoprotein probes, but others also reacted with neoproteoglycan probes. According to the reactivity pattern with probe screening, the one lectin from Oudemansiella platyphylla extract (OPL) bound best with asialotransferrin- and asialoagalactotransferrin-peroxidase probes and was isolated using an asialotransferrin column, but it did not bind with other hybrid glycoprotein or neoproteoglycan probes. OPL, consisting of two polypeptides with high homology in the N-terminal amino acid sequences, exhibited weak hemagglutinating activity. Purified OPL specifically bound the .beta.-GlcNAc probe among various biotinylated polymeric sugar probes, while it exhibited essentially the same binding specificity toward neoglycoconjugate probes as that of the crude extract, showing a preference for the asialobiantennary complex type of N-linked glycans. These results indicate that the neoglycoconjugate probes are valuable in lectin screening. .COPYRGT. 2001 Elsevier Science B.V.

L150 ANSWER 21 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000377244 EMBASE
TITLE: Catalysis of decarboxylation by a preorganized heterogeneous microenvironment: Crystal structures of abzyme 21D8.
AUTHOR: Hotta K.; Lange H.; Tantillo D.J.; Houk K.N.; Hilvert D.; Wilson I.A.
CORPORATE SOURCE: K. Hotta, Department of Molecular Biology, Skaggs Inst. for Chemical Biology, Scripps Research Institute, 10550 North Torrey Pines Road, San Diego, CA 92037, United States
SOURCE: Journal of Molecular Biology, (6 Oct 2000) 302/5 (1213-1225).
Refs: 55
ISSN: 0022-2836 CODEN: JMOBAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Antibody 21D8 catalyzes the solvent-sensitive decarboxylation of 3-carboxybenzisoxazoles. The crystal structure of chimeric Fab 21D8 with and without hapten at 1.61 .ANG. and 2.10 .ANG., respectively, together with computational analysis, shows how a melange of polar and non-polar sites are exploited to achieve both substrate binding and acceleration of a reaction normally facilitated by purely aprotic dipolar media. The striking similarity of the decarboxylase and a series of unrelated esterase antibodies also highlights the chemical versatility of structurally conserved anion binding sites and the relatively subtle changes involved in fine-tuning the immunoglobulin pocket for recognition of different ligands and catalysis of different reactions. (C) 2000 Academic Press.

L150 ANSWER 22 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000018307 EMBASE
TITLE: Isolation of bovine serum albumin fragment P-9 and P-9-mediated fusion of small unilamellar vesicles.

AUTHOR: Sato Y.; Kaneko K.; Mikami K.-I.; Mizugaki M.; Suzuki Y.
CORPORATE SOURCE: Y. Sato, Faculty of Pharmaceutical Sciences, Tohoku University, Aobayama, Aoba-ku, Sendai 980-8578, Japan
SOURCE: Biological and Pharmaceutical Bulletin, (1999) 22/12 (1360-1365).
Refs: 48
ISSN: 0918-6158 CODEN: BPBLEO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Fusion peptide P-9 was isolated from bovine serum albumin by controlled pepsin degradation in the presence of caprylic acid, followed by Sephadex G- 75 gel filtration and ion-exchange chromatography of CM-cellulose. By this procedure, P-9 could be strictly separated from peptic fragment P-Phe, which has a molecular weight close to that of P-9. P-Phe has no fusogenic activity. The addition of P-9 to phosphatidylcholine (PC) liposomes containing cholesterol (Chol) gave rise to an increase of absorption intensity at around pH 4.0. The increase of turbidity by P-9 addition did not decrease with increasing pH, indicating P-9-mediated fusion of PC liposomes. The extent of the fusion of PC liposomes was strongly dependent on the PC chain length and temperature. The membrane fluidity close to the polar head groups of the fatty acyl chains of PC affected markedly the extent of P-9-mediated liposome fusion. However, there was no correlation between membrane fluidity near the hydrophobic end of the fatty acyl chains and the extent of liposome fusion. The rate of liposome fusion was dependent on both lipid composition and PC chain length. These results suggest that a contact or an interaction of P-9 with liposomal membrane occurs in the rigid regions. The character of the membrane-water interface region in the liposome controls a triggering effect for P-9-mediated fusion.

L150 ANSWER 23 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999049417 EMBASE
TITLE: The serum albumin-binding region of streptococcal protein G (BB) potentiates the immunogenicity of the G130-230 RSV-A protein.
AUTHOR: Libon C.; Corvaia N.; Haeuw J.-F.; Nguyen T.N.; Stahl S.; Bonnefoy J.- Y.; Andreoni C.
CORPORATE SOURCE: C. Libon, Centre d'Immunologie, Inst. de Recherche Pierre Fabre, 5 Avenue Napoleon III, 74164 Saint-Julien-en-Genevois Cedex, France. christine.libon@pierre-fabre.com
SOURCE: Vaccine, (5 Feb 1999) 17/5 (406-414).
Refs: 33
ISSN: 0264-410X CODEN: VACCDE
PUBLISHER IDENT.: S 0264-410X(98)00198-4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB BBG2Na is a protein comprising residues 130-230 of the respiratory syncytial virus subgroup A (RSV-A) G protein (G2Na) fused to the albumin-binding domain of streptococcal G protein (BB). BBG2Na was cloned, expressed in Escherichia coli and renaturated. In rodent models, this subunit RSV vaccine adjuvanted in Alhydrogel.RTM. induced specific antibodies and conferred protection to RSV infection. Comparison of the antibody production in a BALB/c mouse model revealed that BBG2Na induced a stronger and earlier G2Na antibody response than G2Na alone, without

altering the IgG subclass distribution. To address the role of the BB part, we explored its carrier properties and showed that it is a Th dependent antigen, generating a more potent G2Na-specific B cell memory response and able to generate Th cells that provide help for G2Na antibody production.

L150 ANSWER 24 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998105600 EMBASE
TITLE: Mechanism of ligand binding to E- and P-selectin analyzed using selectin/mannose-binding protein chimeras.
AUTHOR: Torgersen D.; Mullin N.P.; Drickamer K.
CORPORATE SOURCE: K. Drickamer, Dept. of Biochemistry, University of Oxford, South Parks Rd., Oxford OX1 3QU, United Kingdom. kd@glycob.ox.ac.uk
SOURCE: Journal of Biological Chemistry, (13 Mar 1998) 273/11 (6254-6261).
Refs: 36
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The mechanism of oligosaccharide binding to the selectin cell adhesion molecules has been analyzed by transferring regions of the carbohydrate-recognition domains of E- and P-selectin into corresponding sites in the homologous rat serum mannose-binding protein. Insertion of two basic regions and an adjacent glutamic acid residue leads to efficient binding of HL-60 cells and sialyl-Lewis(x)-conjugated serum albumin. Substitution of glycine for a histidine residue known to stabilize mannose in the binding site of wild type mannose-binding protein results in dramatic loss of affinity for mannose without decreasing binding to sialyl-Lewis(x). The accumulated effect of these changes is to alter the ligand binding selectivity of the domain so that it resembles E-or P-selectin more closely than it resembles the parental mannose-binding domain. Affinity labeling using sialylLewis(x) in which the sialic acid has been mildly oxidized has been used to verify this switch in specificity and to show that the sialic acid-containing portion of the ligand interacts near the sequence Lys-Lys-Lys corresponding to residues 111-113 of E-selectin. The binding of sialyl-Lewis(x)-serum albumin is inhibited dramatically at physiological and higher salt concentrations, consistent with a significant electrostatic component to the binding interaction. The binding characteristics of these gain-of-function chimeras suggest that they contain many of the selectin residues responsible for selective ligand binding.

L150 ANSWER 25 OF 31 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998124138 EMBASE
TITLE: Gene fragment polymerization gives increased yields of recombinant human proinsulin C-peptide.
AUTHOR: Jonasson P.; Nygren P.-A.; Johansson B.-L.; Wahren J.; Uhlen M.; Stahl S.
CORPORATE SOURCE: S. Stahl, Dept. Biochemistry and Biotechnology, Kungliga Tekniska Hogskolan, S-100 44 Stockholm, Sweden. stefans@biochem.kth.se
SOURCE: Gene, (14 Apr 1998) 210/2 (203-210).
Refs: 25
ISSN: 0378-1119 CODEN: GENED6
PUBLISHER IDENT.: S 0378-1119(98)00026-2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry

030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A multimerization strategy to improve yields upon recombinant production of the 31-aa human proinsulin C-peptide is presented. Gene fragments encoding the C-peptide were assembled using specific head-to-tail multimerization. DNA constructs encoding one, three or seven copies of the C-peptide gene, fused to a serum albumin binding affinity tag, were expressed intracellularly in Escherichia coli. The three fusion proteins were produced at similar levels (approximately 50 mg/l) and were proteolytically stable during production. Enzymatic digestion by trypsin-carboxypeptidase B treatment of the fusion proteins was shown to efficiently release native C-peptide, as determined by mass spectrometry, reverse-phase chromatography and a radioimmunoassay. The quantitative yields of C-peptide obtained from the three different fusion proteins suggest that this multimerization strategy could provide a cost-efficient production scheme for the C-peptide, and that this strategy could be useful also for production of other recombinant peptides.

L150 ANSWER 26 OF 31 BIOTECHDS COPYRIGHT 2002 DERWENT INFO AND ISI
ACCESSION NUMBER: 1999-04683 BIOTECHDS
TITLE: New chimeric polypeptide comprising carrier and polypeptide; recombinant ovalbumin and luliberin fusion protein expressed in Escherichia coli, for use as a recombinant immunocontraceptive vaccine
AUTHOR: Reeves J J; Bertrand K P; Zhang Y
PATENT ASSIGNEE: Univ.Washington-State-Res.Found.
LOCATION: Pullman, WA, USA.
PATENT INFO: WO 9904018 28 Jan 1999
APPLICATION INFO: WO 1998-US14983 17 Jul 1998
PRIORITY INFO: US 1997-897527 21 Jul 1997
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1999-132262 [11]
AB A fusion protein (I), containing a whole or partial carrier protein (II), and at least one reproduction-related protein (III) is claimed. Also claimed is a DNA molecule (IV) encoding (I). (I) is administered to a mammal as an immunocontraceptive vaccine, to induce infertility. It has a homogeneous, known structure that is consistent between batches. Also disclosed are **vectors**, including both plasmids and **viruses**, containing (IV), host cells **transformed** by those vectors, and a means of generating antibodies to (III) by administration of (I). (II) is preferably ovalbumin, and (III) is preferably luliberin (LHRH), FSH or LH. (I) preferably contains two or more LHRH peptides inserted into an antigenic region of (II), such as a B-or T-lymphocyte epitope, or an exposed region. (I) was prepared by insertion of plasmid pOVR, encoding ovalbumin, into the Escherichia coli expression vector plasmid pTZ19U. A NheI site was created after codon-97 of the ovalbumin sequence, and an LHRH encoding sequence inserted, to produce plasmid pLHRH. Gene expression was regulated by the phage T7 promoter. (31pp)

L150 ANSWER 27 OF 31 BIOTECHDS COPYRIGHT 2002 DERWENT INFO AND ISI
ACCESSION NUMBER: 1986-02693 BIOTECHDS
TITLE: In vitro and in vivo synthesis of the hepatitis B virus surface antigen and of the receptor for polymerized human serum **albumin** from **recombinant** human adeno viruses; potential vaccine production
AUTHOR: Ballay A; Levrero M; Buendia M A; Tiollais P; Perricaudet M
CORPORATE SOURCE: Inst.Pasteur

LOCATION: Institut de Recherches Scientifiques sur le Cancer, Centre National de la Recherche Scientifique, 7, rue Guy Moquet, 94800 Villejuif, France.
SOURCE: EMBO J.; (1985) 4, 13B, 3861-65
CODEN: EMJODG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An adeno **virus vector** for expression of foreign proteins under the control of the adeno virus E1a promoter has been developed. Plasmid pE1a (TaqI), containing the promoter and the beginning of the coding sequence of the E1a region, was treated by deletion of the HaeIII-PvuII fragment from the latter part of E1a to give pAB1, containing ClaI and HindIII restriction sites. The BglI-BamHI restriction fragment of SV40 DNA was inserted into pAB1 to give pK4. This plasmid was used to express hepatitis B virus (HBV) coding sequences. 2 Recombinant plasmids, pK4S(X-B) and pK4S(M-B), harboring the S gene or the pre-S region and the S gene of HBV under the control of the Eia promoter, were used to construct 2 recombinant adeno viruses by ligation of PstI-ClaI restriction fragments with Ad5 vector. Ad5-**transformed** human cells 293 were **transfected**, and AdS(X-B) and AdS(M-B) were obtained. The viruses directed the synthesis of HBV surface antigen (HBsAg). In the presence of the pre-S region in the virus, the synthesis of particles carrying the receptor for polymerized human serum **albumin** (pHSA) was seen. **Recombinant** adeno virus may be useful as a live vaccine. (30 ref)

L150 ANSWER 28 OF 31 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2002-055149 [07] WPIDS
DOC. NO. CPI: C2002-015688
TITLE: Stable plastid **transformation** and expression **vector** competent for stably **transforming** a plastid genome for expression of heterologous genes, e.g. insulin.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): DANIELL, H
PATENT ASSIGNEE(S): (AUBU) UNIV AUBURN; (UYFL-N) UNIV CENT FLORIDA
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001072959	A2	20011004	(200207)*	EN	305

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001076813 A 20011008 (200208)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001072959	A2	WO 2001-US6288	20010228
AU 2001076813	A	AU 2001-76813	20010228

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001076813	A Based on	WO 200172959

PRIORITY APPLN. INFO: US 2001-185987 20010223; US 2000-185987P 20000301; US 2001-263424P 20010123; US 2001-263473P 20010123; US 2001-263668P 20010123

AB WO 200172959 A UPAB: 20020306

NOVELTY - A stable plastid **transformation** and expression **vector** competent for stably **transforming** a plastid genome, is new.

DETAILED DESCRIPTION - A stable plastid **transformation** and expression **vector** competent for stably **transforming** a plastid genome, is new, which comprises an expression cassette comprising as operably linked components in the 5' to 3' direction of translation:

(a) a promoter operative in the plastid,

(b) a selectable marker sequence,

(c) a heterologous DNA sequence coding for a biopolymer-proinsulin fusion gene, a cholera toxin B-subunit-proinsulin fusion gene, a plastid DNA fragment comprising a 5'UTR sequence positioned upstream of the promoter to enhance translation of proinsulin protein, a Cry2aA2 operon which comprises two open reading frames (ORFs) where the ORF immediately upstream of Cry2aA2 codes for a putative chaperonin, a cholera toxin B-subunit-plastid modified proinsulin (PtPris) fusion wherein its nucleotide sequence is modified such that the codons are optimized for plastid expression, cholera toxin B-subunit-mini-proinsulin (Mpris) fusion where its codons are optimized for plastid expression, a synthetic protein-base polymer (PBP) fused to a biologically active molecule, an interferon gene, a insulin-like growth factor gene, a human serum **albumin** (HSA) gene, or a biopolymer **fusion** gene,

(d) a transcription termination region functional in the plastid, and

(e) flanking, each side of the expression cassette, flanking DNA sequences which are homologous to a DNA sequence inclusive of a spacer sequence of the target plastid genome, whereby stable integration of the heterologous coding sequence into the plastid genome of the target plant is facilitated throughout homologous recombination of the flanking sequence with the homologous sequence in the target plastid genome.

INDEPENDENT CLAIMS are also included for the following:

(1) a stably **transformed** plant which comprises plastid stably **transformed** with the above **vector**, or the progeny or seeds of it;

(2) a process for stably **transforming** a higher target plant species which comprises introducing into the plastid genome of the plant the above **vector**; and

(3) a **transformed** and edible tobacco or alfalfa plant of (1);

(4) a process for recovering a biopolymer by a one step extraction and purification by using the reversible property of the biopolymer; and

(5) a process for recovery of a synthetic protein-base polymer (PBP) fused with a biologically active molecule by one step extraction and purification by using the reversible property of the biopolymer of (4).

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The **vector** can be used to stably **transform** a plant. It can be used to produce edible tobacco, or alfalfa plants (all claimed).

ADVANTAGE - By producing the heterologous genes in an edible plant, the proteins can be orally delivered to patients that require them, e.g. insulin to diabetics, without the need for injections.

Dwg.0/10

L150 ANSWER 29 OF 31 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-175732 [18] WPIDS
DOC. NO. CPI: C1996-055505
TITLE: **Fusion** protein comprising human serum **albumin** contg. peptide inserted at arbitrary

position - useful for, e.g. inhibiting cancer metastasis.
DERWENT CLASS: B04 D16
PATENT ASSIGNEE(S): (ASAG) ASAHI GLASS CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 08053500	A	19960227	(199618)*		24

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 08053500	A	JP 1994-209368	19940811

PRIORITY APPLN. INFO: JP 1994-209368 19940811
AB JP 08053500 A UPAB: 19960503
A fusion protein, prepared by introducing peptide(s) into at least one arbitrary position in a polypeptide chain of human serum albumin, is new. Also claimed are: (1) a gene (I) encoding the fusion protein; (2) a recombinant **vector** contg. (I); and (3) a host cell **transformed** with the **vector** of (2) and capable of producing the fusion protein.

USE - The gene is used for production of a fusion protein capable of demonstrating its physical activity sufficiently without destruction of the stereostructure of human serum albumin protein.

ADVANTAGE - A fusion protein eg. a fusion protein for inhibiting cancer metastasis, which could be prepared in the prior art only by a combination of a chemical synthetic method and a binding method, can be produced directly and efficiently for the first time by recombinant DNA technology, thus realising the stable supply in industrial scale processes of a fusion protein for inhibiting cancer metastasis as pharmaceuticals.
Dwg.0/8

L150 ANSWER 30 OF 31 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1995-354277 [46] WPIDS
DOC. NO. CPI: C1995-154927
TITLE: **Fusion** gene coding for **albumin** fused to human apo lipoprotein E - also **vectors** and **transformed** yeast for prepn. of fusion protein as intermediate for drugs, reagents and apo lipoprotein E.
DERWENT CLASS: B04 D16
PATENT ASSIGNEE(S): (BEPP-I) BEPPU T
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 07241196	A	19950919	(199546)*		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 07241196	A	JP 1994-58270	19940304

PRIORITY APPLN. INFO: JP 1994-58270 19940304
AB JP 07241196 A UPAB: 19951122
A fusion gene in which albumen and human apolipoprotein E-like gene are linked together is new. Also claimed are : (1) a plasmid in which the

above fusion gene is inserted and (2) a yeast **transformed** by the above plasmid.

USE - The fusion protein is useful as an intermediate for the synthesis of reagents, drugs and apolipoprotein E-like protein.
Dwg.0/0

L150 ANSWER 31 OF 31 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1989-229526 [32] WPIDS
DOC. NO. CPI: C1989-101850
TITLE: Fusion protein capable of selective binding to serum **albumin** - obtd. by gene **fusion**, pref. using gene coding for protein G of streptococcus strain G148.
DERWENT CLASS: B04 D16
INVENTOR(S): UHLEN, M; ABRAHMSEN, L; NYGREN, P
PATENT ASSIGNEE(S): (ABRA-I) ABRAHMSEN L; (NYGR-I) NYGREN P A; (NYGR-I) NYGREN P; (UHLE-I) UHLEN M
COUNTRY COUNT: 14
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 327522	A	19890809	(198932)*	EN	13
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
SE 8800378	A	19890806	(198939)		
JP 02005887	A	19900110	(199008)		
SE 501169	B	19941128	(199502)		
EP 327522	B1	19951213	(199603)	EN	16
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
DE 68925044	E	19960125	(199609)		
ES 2080759	T3	19960216	(199614)		
JP 3026812	B2	20000327	(200020)		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 327522	A	EP 1989-850031	19890202
JP 02005887	A	JP 1989-24142	19890203
SE 501169	B	SE 1988-378	19880205
EP 327522	B1	EP 1989-850031	19890202
DE 68925044	E	DE 1989-625044	19890202
		EP 1989-850031	19890202
ES 2080759	T3	EP 1989-850031	19890202
JP 3026812	B2	JP 1989-24142	19890203

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 68925044	E	Based on	EP 327522
ES 2080759	T3	Based on	EP 327522
JP 3026812	B2	Previous Publ.	JP 02005887

PRIORITY APPLN. INFO: SE 1988-378 19880205
AB EP 327522 A UPAB: 19930923
Method of producing a fusion protein or polypeptide capable of selective binding to serum albumin (SA) comprises (a) constructing a recombinant **vector** comprising a first DNA sequence coding for a SA binding polypeptide fragment and operatively linked to a second DNA sequence coding for pref. protein or polypeptide, (b) transferring a host with the **vector** such that the combined DNA sequence coding for the fusion protein can be expressed by the host and culturing the **transformed**

host and (c) isolating the fusion protein. Also claimed is the recombinant **vector** of (a) and a host **transformed** by the recombinant **vector**.

USE/ADVANTAGE - Due to the albumin-binding ability the produced protein can easily be isolated with high efficiency by affinity chromatography using SA on a carrier. The carrier-bound fusion prod. may be used as such e.g. if pref. protein is an enzyme, or it may be released from the carrier, either as a whole including the albumin-binding part or only pref. protein through cleavage.
0/10

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